Amendments to the Claim:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1 (currently amended). A process for production of a purified recombinant mature polypeptide with arylsulfatase A (ASA) activity in a continuous cell culture system, the process comprising:

i) continuously culturing a mammalian cell capable of ~~producing~~ secreting said ~~arylsulfatase A~~ mature polypeptide into a liquid culture medium; and

ii) ~~concentrating,~~ purifying ~~and formulating~~ the ~~recombinant ASA~~ mature polypeptide by a purification process comprising one or more steps of affinity chromatography and/or ion exchange chromatography,

wherein the ~~concentration and purification~~ process of (ii) comprises a polishing step including a passive step, wherein the mature polypeptide with arylsulfatase A activity passes through a cation exchange chromatography resin or membrane and/or affinity chromatography resin without binding thereto, and an active step, wherein the mature polypeptide with arylsulfatase A activity is detained within and subsequently eluted from an anion exchange membrane or resin, and wherein the cation exchange chromatography resin or membrane and the anion exchange ~~membrane or resin~~ resin or membrane are coupled or connected in a series,

wherein said mammalian cell comprises a nucleotide sequence which encodes a polypeptide comprising (a) SEQ ID NOs:2 or 4 or (b) a mutant sequence at least 95% identical to SEQ ID NOs:2 or 4, and wherein said mature polypeptide~~, or~~ is a post-translationally modified product thereof that is produced and secreted by said cell, and has arylsulfatase A activity, and wherein the continuous culturing is for a period of at least one week.

2-7 (cancelled).

8 (previously presented). A process according to claim 1, wherein the mammalian cells are of human or primate origin.

9 (currently amended). A process according to claim 1, wherein the ~~concentration and purification~~ process of ii) comprises one or more steps of Expanded Bed Chromatography.

10 (cancelled).

11 (currently amended). A process according to claim 1, wherein the ~~concentration and purification~~ process of ii) comprises the following steps:

II) ~~contacting an arylsulfatase A containing~~ introducing a supernatant containing said mature polypeptide into ~~on~~ an equilibrated chromatography column and eluting one or more fraction(s) containing ~~arylsulfatase A~~ said mature polypeptide;

III) loading the fraction(s) from step II on another equilibrated chromatography column and eluting one or more fraction(s) containing ~~arylsulfatase A~~ said mature polypeptide;

IV) buffer exchange of ~~the arylsulfatase A~~ said mature polypeptide present in the fraction(s) from step III by tangential flow filtration;

V) polishing the preparation of ~~arylsulfatase A~~ said mature polypeptide from step IV in one or two or more successive steps, each step comprising loading the preparation on an equilibrated chromatography columns and eluting one or more fraction(s) containing ~~arylsulfatase A~~ said mature polypeptide, wherein said polishing comprises a passive step, in which said mature polypeptide passes through a cation chromatography resin or membrane and/or affinity chromatography resin without binding thereto, and an active step, wherein said polypeptide is detained within and subsequently eluted from an anion exchange membrane or resin; and

VI) passing the fraction(s) from step V through a viral reduction filter and/or inactivating virus in said fraction(s) with a virus inactivating agent~~;~~

~~VII) formulating the fraction(s) from step VI in order to obtain a preparation of arylsulfatase A in a suitable formulation buffer;~~

~~VIII) optionally filling the formulated preparation of arylsulfatase A into a suitable container and freeze-drying the sample~~.

12 (currently amended). A process according to claim 11, further comprising an initial step I) of concentrating the ~~arylsulfatase A~~ mature polypeptide by tangential flow filtration.

13 (previously presented). A process according to claim 11, wherein the chromatography column used in step II of the purification process is an anion exchange column.

14 (original). A process according to claim 13, wherein said anion exchange column is a DEAE Sepharose column or a DEAE Streamline column.

15 (previously presented). A process according to claim 11, wherein the chromatography column used in step III of the purification process is a hydrophobic interaction column.

16 (previously presented). A process according to claim 11, wherein purification of the sample in step IV of the purification process is accomplished by tangential flow filtration.

17 (cancelled).

18 (previously presented). A process according to claim 11, wherein the inactivating agent is a detergent.

19-42 (cancelled).

43 (currently amended). The process of claim 1 wherein the ~~arylsulfatase~~ mature polypeptide has a specific arylsulfatase A activity of at least 20 units/mg.

44 (previously presented). The process of claim 1 wherein the mutant sequence is at least 96% identical to SEQ ID NO:2 or 4.

45 (previously presented). The process of claim 1 wherein the mutant sequence is at least 97% identical to SEQ ID NO:2 or 4.

46 (previously presented). The process of claim 1 wherein the mutant sequence is at least 98% identical to SEQ ID NO:2 or 4.

47 (previously presented). The process of claim 1 wherein the mutant sequence is at least 99% identical to SEQ ID NO:2 or 4.

48 (previously presented). The process of claim 1 wherein the polypeptide comprises SEQ ID NOs:2 or 4.

49 (previously presented). The process of claim 1 wherein the produced arylsulfatase A consists of SEQ ID NO:3.

50 (cancelled).

51 (previously presented). The process of claim 1 wherein the encoded polypeptide, when aligned by sequence alignment software to SEQ ID NO:2 or 4, has a cysteine in the position aligned with Cys-69 in SEQ ID NO: 2 or Cys-51 in SEQ ID NO:4.

52 (previously presented). The process of claim 51 wherein a linear sequence of five amino acids within said polypeptide, and including said cysteine, is identical to the aligned sequence of five amino acids in SEQ ID NO:2 or SEQ ID NO:4.

53 (previously presented). The process of claim 51 wherein a linear sequence of nine amino acids within said polypeptide, and including said cysteine, is identical to the aligned sequence of nine amino acids in SEQ ID NO:2 or SEQ ID NO:4.

54 (previously presented). The process of claim 51 wherein a linear sequence of twenty amino acids within said polypeptide, and including said cysteine, is at least 95% identical to the aligned sequence of twenty amino acids in SEQ

ID NO:2 or SEQ ID NO:4.

55 (previously presented). The process of claim 51 wherein a linear sequence of twenty amino acids within said polypeptide, and including said cysteine, is identical to the aligned sequence of twenty amino acids in SEQ ID NO:2 or SEQ ID NO:4.

56 (Previously presented). The process of claim 51 wherein the encoded polypeptide comprises at least one putative N-glycosylation site.

57 (Previously presented). The process of claim 51 wherein at least putative N-glycosylation site is phosphorylable.

58 (Previously presented). The process of claim 51 wherein the encoded polypeptide, when aligned by sequence alignment software to SEQ ID NO:2 or 4, has asparagine in the positions aligned with Asn-158 and Asn=350 in SEQ ID NO: 2 or Asn-140 and Asn-332 in SEQ ID NO:4.

59 (Previously presented). The process of claim 58 wherein the encoded polypeptide, when aligned by sequence alignment software to SEQ ID NO:2 or 4, has asparagine in the position aligned with Asn-184 in SEQ ID NO: 2 or Asn-166 in SEQ ID NO:4.

60 (New). The process of claim 1, wherein said continuous culturing is for a period of at least two weeks.

61 (New). The process of claim 1, wherein said continuous culturing is for a period of at least three weeks.

62 (New). The process of claim 1, wherein said continuous culturing is for a period of at least four weeks.

63 (New). The method of claim 1 wherein said continuous culturing is carried out in a cell culture system comprising one or more bioreactors, said cells being in said bioreactor(s), said system comprising means for collecting medium comprising said polypeptide, and a cell retention device for retaining cells in said bioreactor(s) when said medium is collected, and said system comprising means for

adding fresh medium.

64 (New). The method of claim 63 wherein said cell retention device is at least 95% efficient.

65 (New). The method of claim 63 wherein medium comprising said polypeptide is collected, while retaining cells in said bioreactor(s), at least once prior to the conclusion of said culturing.

66 (New). The method of claim 65 in which medium comprising said polypeptide is collected at least daily.

67 (New). A method of preparing a pharmaceutically acceptable formulation comprising a polypeptide with ASA activity, said method comprising purifying said polypeptide by the method of claim 1, and formulating a pharmaceutically acceptable formulation comprising said polypeptide.

68 (New). The method of claim 11, further comprising (VII) formulating the fraction(s) from step VI in order to obtain a preparation of said polypeptide in a suitable formulation buffer.

69 (New). The method of claim 68, further comprising

VIII) optionally filling the formulated preparation of said polypeptide of step VII into a suitable container and freeze-drying the sample.